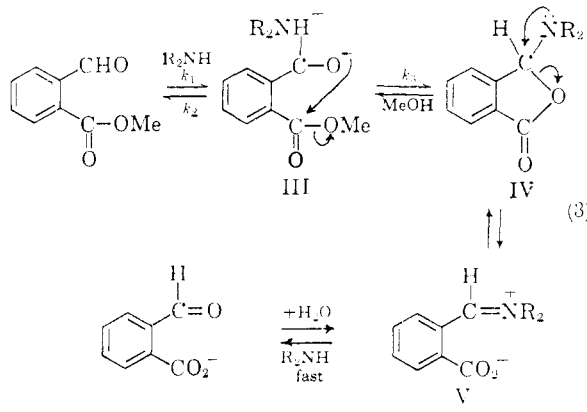
set of data is found, yielding $k_1 = 21.5\ M^{-1}$, $k_2 = 0.24$ and $k_3 = 0.033$ sec.$^{-1}$ at μ 1.0 and pH 8.7. These data yield the calculated solid line in Fig. 1, in good agreement with experiment.[7] The calculated and experimental curves for the other data are in reasonable agreement.

On the basis of the above evidence mechanism (3) for the morpholine catalysis can be postulated.[8,9]



The morpholine catalysis (like the hydroxide ion catalysis) is, on this basis, an example of nucleophilic catalysis of ester hydrolysis in which the nucleophile does not react directly with the ester linkage to form an unstable intermediate (the usual type of nucleophilic catalysis) but rather reacts with a neighboring group to form an unstable intermediate which leads eventually to the hydrolytic products and the regeneration of the catalyst. A similar example in the hydrolysis of a keto-substituted phosphoric acid ester is consistent with this interpretation.[10]

(7) The theoretical curve was calculated using an Applied Dynamics AD-232PB analog computer by Dr. Kenneth A. Connors of the School of Pharmacy, University of Wisconsin. It is assumed in this computation that the intermediate has an extinction coefficient at 290 mμ of approximately two-thirds that of the reactant.

(8) The constant k_1 is increased and k_3 is decreased by increasing μ, as predicted by eq. 3.

(9) Compound III is analogous to an intermediate in Schiff base formation: E. H. Cordes and W. P. Jencks, *J. Am. Chem. Soc.*, **84**, 832 (1962).

(10) F. Ramirez, B. Hansen and N. B. Desai, *ibid.*, **84**, 4588 (1962).

(11) Alfred P. Sloan Foundation Research Fellow.

(12) National Science Foundation Postdoctoral Fellow on leave from Amherst College.

(13) The authors acknowledge the assistance of Drs. F. J. Kezdy and G. E. Clement with the morpholine kinetics.

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THE STRUCTURE OF CYCLOBUXINE

Sir:

The medicinal properties of *Buxus sempervirens* L. have been known since ancient times; extracts of the plant have been used in the treatment of a wide variety of diseases, including malaria and venereal disease.[1] More recently, an alkaloidal extract of the plant has been reported to possess antitubercular properties.[2] Earlier studies have indicated the multicomponent nature of the alkaloid extract.[1,3-6] Evidence is presented herewith for assignment of structure I to an alkaloid isolated from the acetone-insoluble portion of the strong base fraction, for which we propose the name *cyclobuxine*.[7] Cyclobuxine represents a novel type of steroidal alkaloid; it appears to be the first recognized to contain a cyclopropane ring and the first with a substitution pattern at C-4 and C-14 which is intermediate in the biogenetic scheme, between lanosterol- and cholesterol-type steroids.

Cyclobuxine (I), $C_{25}H_{42}ON_2$, m.p. 245–247° dec., $[\alpha]^{23}D$ + 98°,[8] shows λ_{max} 6.09, 11.20 μ[8] (terminal methylene) and n.m.r. peaks[9] 5.20 and 5.43 (2H, doublets, $J < 1$ c./s.; terminal methylene), 5.92 (1H, octuplet, J's 3, 7, 9.5 c./s.; CH_2–C*H*OH–CH), 7.53 and 7.57 (6H, two NCH_3), 8.87 and 9.03 (6H, two tertiary CH_3), 8.92 (3H, doublet, J 6 c./s.; one sec. CH_3) and 9.72 and 9.95 τ (2H, doublets, J 4 c./s.; cyclopropyl methylene). Cyclobuxine was converted to several crystalline derivatives: *e.g.*, the dihydrobromide, $C_{25}H_{44}ON_2Br_2$, m.p. 288–292° dec.; the N,N'-dimethyl derivative,[3] $C_{27}H_{46}ON_2$, m.p. 204–205° dec., $[\alpha]^{25}D$ + 99°, n.m.r. peaks at 5.07, 5.38, 5.98, 8.87, 9.03, 9.72, 9.97 (as for cyclobuxine), 5.60 (1H, OH), 7.68 and 7.77 (12H, two $N(CH_3)_2$) and 9.13 τ (3H, doublet, J 6.5 c./s.; sec. CH_3 near $N(CH_3)_2$); the N,N'-dimethyl-O-acetate,[3] $C_{29}H_{48}O_2N_2$, m.p. 173–175°, $[\alpha]^{25}D$ + 69°, λ_{max} 5.81 μ, n.m.r. peaks at 4.95 (1H, octuplet; CH_2-C*H*OAc-CH), 8.03 (3H, CH_3COO–); the triacetate,[3] $C_{31}H_{48}O_4N_2$, m.p. 256–258° dec., $[\alpha]^{24}D$ – 12°, λ_{max} 5.78, 6.14, 11.08μ; the dihydro derivative,[3] $C_{25}H_{44}ON_2$, m.p. 208–209°, $[\alpha]^{25}D$ + 46°, infrared showed no bands at 6.09 or 11.20 μ, n.m.r. peaks at 9.22 (3H, doublet, J 7 c./s.; new sec. CH_3), 9.43 and 9.73 τ (2H, cyclopropyl methylene).

The gross skeletal structure was indicated by the structures suggested for the products of selenium dehydrogenation: an 8-methyl-1,2-cyclopentenophenanthrene (II), $C_{21}H_{22}$, m.p. 145–147°, trinitrobenzene complex, $C_{27}H_{25}O_6N_3$, m.p. 165–168°; the corresponding 5-methyl-1,2-cyclopentenoanthracene (III), $C_{21}H_{22}$, m.p. 110–112°, trinitrobenzene complex, $C_{27}H_{25}O_6N_3$, m.p. 168–169°; and two naphthalenes, IV, $C_{21}H_{28}$, m.p. 134–135°, trinitrobenzene complex, $C_{27}H_{31}O_6N_3$, m.p. 143–145°; and V, $C_{22}H_{28}$, m.p. 111–117°, trinitrobenzene complex, $C_{28}H_{31}O_6N_3$, m.p. 139–141°. The hydrocarbons were characterized by analysis, infrared, ultraviolet,

(1) E. Schlittler, K. Heusler and W. Friedrich, *Helv. Chim. Acta*, **32**, 2209 (1949).

(2) L. E. Weller, C. T. Redemann, R. V. Gottshall, J. M. Roberts, E. H. Lucas, and H. M. Sell, *Antibiotics and Chemotherapy*, **3**, 603 (1953); Merck & Co., Inc., British Patent 782,469 (1957).

(3) K. Heusler and E. Schlittler, *Helv. Chim. Acta*, **32**, 2226 (1949).

(4) W. Friedrich and E. Schlittler, *ibid.*, **33**, 873 (1950).

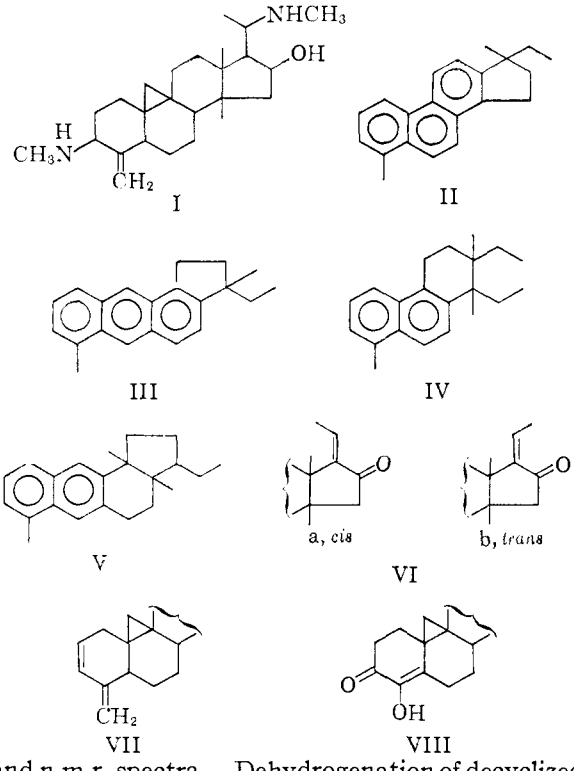
(5) E. Schlittler and W. Friedrich, *ibid.*, **33**, 878 (1950).

(6) K. S. Brown, Jr., and S. M. Kupchan, *J. Chromatography*, **9**, 71 (1962).

(7) Cyclobuxine is "III," the alkaloid of R_f 0.76 in Fig. 2 of reference 6. It is most probably the same as "Alkaloid A" of reference 3; although no comparison sample of "A" is available, the physical constants of cyclobuxine and its derivatives correspond closely to those of "A" and the respective derivatives.

(8) All rotations and infrared spectra are in chloroform.

(9) All n.m.r. spectra were determined on a Varian Associates recording spectrometer (A-60) at 60 Mc. in deuterated chloroform or carbon tetrachloride. Chemical shifts are reported in τ values (p.p.m.) [G. V. D. Tiers, *J. Phys. Chem.*, **62**, 1151 (1958)]. We thank Mr. Roy Matsuo and Mr. Arnold Krubsack for these determinations.



and n.m.r. spectra. Dehydrogenation of decyclized material (in which the cyclopropane had been opened in the usual manner) gave *only phenanthrene-related products.*

Ozonolysis of N,N′-diacyl derivatives[10] gave α-acylamino-ketones which had lost one carbon atom and which gave negative Zimmermann tests.[11] Decyclization of cyclobuxine and various derivatives with hydrogen chloride in chloroform gave mixtures showing n.m.r. peaks for a new tertiary methyl group and a new vinyl hydrogen; the new double bonds resisted hydrogenation. Chromic acid or manganese dioxide oxidation of N,N′-diacyl derivatives of dihydrocyclobuxine gave cyclopentanones (λ_{max} 5.78 μ) showing positive Zimmermann tests. It was not possible to move the double bonds produced by decyclization into conjugation with the keto-groups produced by manganese dioxide oxidation. The oxidation product of dihydrocyclobuxine[12] (N,N′-dibenzoyl derivative, $C_{39}H_{50}O_3N_2$, m.p. 281–283° dec., $[\alpha]^{21}D$ — 53°) rapidly eliminated methylamine in basic solution to give two *cisoid* cyclopentenones (VIa and VIb): λ_{max} 5.85, 6.09 μ; λ_{max}^{EtOH} 244 mμ (ϵ 7,700); n.m.r. peaks for *cis*[13] isomer, VIa, m.p. 149–152°, 3.53 (1H, quadruplet, J 7.5 c./s.; vinyl proton coupled with CH_3), 7.60 (3H, NCH_3), 8.19 (3H, doublet, J 7.5 c./s.; vinyl CH_3), 8.68, 9.05 (6H, 2 tertiary CH_3), 9.19 (3H, doublet, J 7 c./s.; secondary CH_3), and 9.34 and 9.67 τ (2H, cyclopropyl methylene); n.m.r. peaks for *trans* isomer, VIb, m.p. 134–137°, 4.35 (1H, quadruplet, J 7 c./s.), 7.62 (3H), 7.92 (3H, doublet, J 7 c./s.), 8.77 (3H), 9.08 (3H), 9.21 (3H, doublet, J 7 c./s.), and 9.33 and 9.69 τ (2H)[14]; dihydro-N-benzoyl derivative, $C_{31}H_{43}O_2N$, m.p. 220–223°. The ketones still gave positive Zimmermann tests.

Hofmann degradation of N,N′-dimethylcyclobuxine monomethiodide,[3] $C_{28}H_{49}ON_2I$, m.p. 224–227° dec., yielded N,N′-dimethylcyclobuxine (10–20%) and VII[3] (70%), $C_{25}H_{39}ON$, m.p. 169–170°, $[\alpha]^{22}D$ + 170°; λ_{max} 3.00, 6.10, 6.25, 11.15, 11.30 μ; λ_{max}^{EtOH} 229.5 mμ (ϵ 16,600), shoulders at 225, 238 mμ; n.m.r. peaks at 3.60–4.60 (2H, complex splitting; vinyl protons), 5.34 (2H, terminal methylene), 6.06 (1H, octuplet; CHOH), 6.80 (1H, OH), 7.73 (6H, $N(CH_3)_2$), 8.87, 9.03, 9.14 (9H, 3 CH_3, as in N,N′-dimethylcyclobuxine), 9.72 and 9.90 τ (2H, doublets, J 4 c./s.; cyclopropyl methylene); *O*-monoacetate, λ_{max} 5.80 μ; tetrahydro derivative,[3] $C_{25}H_{43}ON$, m.p. 161–164°, $[\alpha]^{23}D$ + 36°. VII showed no tendency to aromatize upon chloranil dehydrogenation.

Base treatment of the ozonolysis product of cyclobuxine[12] (dihydrochloride, $C_{24}H_{40}O_2N_2 \cdot 2HCl \cdot H_2O$, dec. > 225°) yielded VIII, a diosphenol showing additional conjugation, λ_{max} 2.91 (strong), 6.04, 6.18 μ; λ_{max}^{EtOH} 296.5 mμ (ϵ 9,000), $\lambda_{max}^{0.1\,N\,NaOH}$ 343.5 mμ (ϵ 6,500); triacetate, $C_{29}H_{41}O_6N$, m.p. 245–250° dec., λ_{max} 5.67, 5.78, 5.97, 6.14 μ; λ_{max}^{EtOH} 277 mμ (ϵ 12,600). The corresponding diosphenol from decyclized cyclobuxine showed λ_{max} 2.91, 6.00 μ; λ_{max}^{EtOH} 277 mμ (base, 322 mμ); triacetate, λ_{max} 5.68, 5.78, 5.96, 6.13 μ, λ_{max}^{EtOH} 247 mμ (ϵ 12,500).[15,16,17]

(10) Non-acylated derivatives were not attacked by ozone or peracid, indicating the close proximity of an amino function to the double bond.

(11) W. Zimmermann, *Z. physiol. Chem.*, **300**, 141 (1955).

(12) Obtained *via* the N,N′-di-*p*-nitrobenzylcarbamate.

(13) *Cf.* L. F. Fieser and M. Fieser, *Experientia*, **4**, 285 (1948).

(14) The configurations of VIa and VIb were assigned on the basis of the n.m.r. spectra; *cf.* L. M. Jackman and R. H. Wiley, *J. Chem. Soc.*, 2881 (1960).

(15) *Cf.* the analogous diosphenol from cholesterol, λ_{max}^{EtOH} 278 mμ; acetate, λ_{max}^{EtOH} 247 mμ (L. F. Fieser and R. Stevenson, *J. Am. Chem. Soc.*, **76**, 1728 (1954)), and that from cevagenine, λ_{max}^{EtOH} 278 mμ (base, 320 mμ) (E. Sundt, O. Jeger and V. Prelog, *Chem. and Ind.*, 1365 (1953).

(16) Satisfactory analyses have been obtained for products with cited empirical formulas. We thank Mr. Joseph Alicino, Metuchen, N. J., for the analyses.

(17) We gratefully acknowledge the kind assistance of the Ciba Pharmaceutical Company in procurement and large-scale extraction of plant material, and thank especially Drs. Emil Schlittler, Daniel Dickel and Karl Heusler for their kind interest and co-operation. The investigation was supported in part by research grants from the National Institutes of Health (H-2952 and CY-4500).

(18) Cooperative National Science Foundation Predoctoral Fellow in Chemistry, 1960–1962.

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π-ALLYL-IRON TRICARBONYL CATIONS

Sir:

We wish to report the preparation of a new series of stable salts of π-allyl-iron tricarbonyl cations. The allyl group previously has been found to function as a π-type ligand in complexes of Mn, Co, Ni, and Pd,[1] also in the covalent molecule methylallyl-chloro-iron tricarbonyl[2] and in the per-

(1) W. R. McClellan, H. H. Hoehn, H. N. Cripps, E. L. Muetterties and B. W. Howk, *J. Am. Chem. Soc.*, **83**, 1601 (1961); R. F. Heck and D. S. Breslow, *ibid.*, **83**, 1097 (1961); J. M. Rowe, *Proc. Chem. Soc.*, 66 (1962); G. Wilke and B. Bogdanovic, *Angew. Chem.*, **73**, 756 (1961), and references contained therein.

(2) F. J. Impastato and K. G. Ihrman, *J. Am. Chem. Soc.*, **83**, 3726 (1961).